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(54) **MODULATORS OF PIN1 ACTIVITY AND USES THEREOF**

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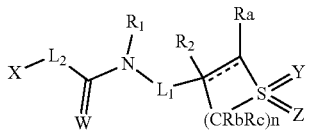
(57) **ABSTRACT**

Disclosed herein are compounds comprising an electrophilic moiety and rigid moiety for use in modulating an activity of Pin1. The rigid moiety comprises at least one functional group that is capable of forming hydrogen bonds with hydrogen atoms, wherein the electrophilic moiety and the rigid moiety are arranged such that the electrophilic moiety is capable of covalently binding to the Cys113 residue of Pin1, and the rigid moiety is capable of forming hydrogen bonds with the Gln131 and His 157 residues of Pin1. Further disclosed are novel compounds having Formula Id:

Formula Id



wherein the dashed line, W, X, Y, Z, Ra-Rc, R_1, R_2, L_1, L_2 and n are as defined herein, and libraries comprising such compounds. Further disclosed are methods of identifying a compound capable of modulating an activity of Pin1, by screening a library of compounds.

Specification includes a Sequence Listing.